peri-Adventitial delivery of smooth muscle cells in porous collagen scaffolds for treatment of experimental abdominal aortic aneurysm.

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Public Summary:
Abdominal aortic aneurysm (AAA) is associated with the loss of vascular smooth muscle cells (SMCs) within the vessel wall. Direct delivery of therapeutic cells is challenging due to impaired mechanical integrity of the vessel wall. We hypothesized that porous collagen scaffolds can be an effective vehicle for the delivery of human-derived SMCs to the site of AAA. The purpose was to evaluate if the delivery of cell-seeded scaffolds can abrogate progressive expansion in a mouse model of AAA. Collagen scaffolds seeded with either primary human aortic SMCs or induced pluripotent stem cell derived-smooth muscle progenitor cells (iPSC-SMPs) had >80% in vitro cell viability and >75% cell penetrance through the scaffold's depth, while preserving smooth muscle phenotype. The cell-seeded scaffolds were successfully transplanted onto the murine aneurysm peri-adventitia on day 7 following AAA induction using pancreatic porcine elastase infusion. Ultrasound imaging revealed that SMC-seeded scaffolds significantly reduced the aortic diameter by 28 days, compared to scaffolds seeded with iPSC-SMPs or without cells (acellular scaffold), respectively. Bioluminescence imaging demonstrated that both cell-seeded scaffold groups had cellular localization to the aneurysm but a decline in survival with time. Histological analysis revealed that both cell-seeded scaffold groups had more SMC retention and less macrophage invasion into the medial layer of AAA lesions, when compared to the acellular scaffold treatment group. Our data suggest that scaffold-based SMC delivery is feasible and may constitute a platform for cell-based AAA therapy.

Scientific Abstract:
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